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Dimethyl Cyan

Carboxethyl Cyclopentanone

Chemistry

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DIMETHYL CYAN CARBOXETHYL
CYCLOPENTANONE

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BY

WILLIS O. GORDON

THESIS FOR THE DEGREE OF BACHELOR OF SCIENCE

IN CHEMISTRY

IN THE

COLLEGE OF SCIENCE

OF THE

UNIVERSITY OF ILLINOIS

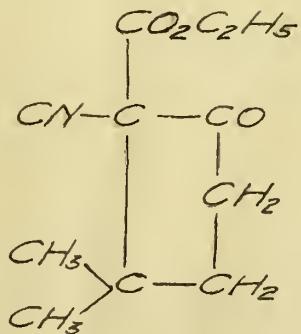
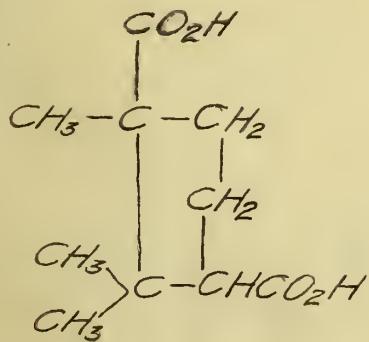
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DIMETHYL-CYAN-CARBOXETHYL-CYCLOPENTANONE.

Camphor has given rise to a large amount of research in the past decade, and while its structure is practically agreed upon, the numerous side plays of scientific inquiry are extremely interesting and afford opportunity for development of research spirit and investigational ability connected with more important discussions. The investigation has been confined mostly to the acids derived from camphor, looking forward to the direct synthesis of camphor itself, and has furnished a fertile field for discussion and disagreement.

Upon sight there is quite a little resemblance between the structure of camphoric acid and dimethylcyanocarboxethylicyclopentanone and a synthesis of the former through the latter seems possible from their formulas:

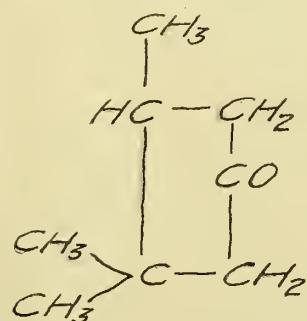
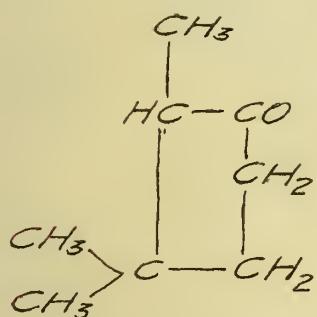


E. B. Harris, (Am. Chem. J., Vol. 18, p. 692), treated dihydro-ciscampholytic acid, first converting it into the free amine, and then treating the portion that he would have converted into the alcohol with Beckman's mixture of sulphuric acid and potassium pyrochromate, forming the ketone and from the ketone, the oxime with hydroxylamine chloride.

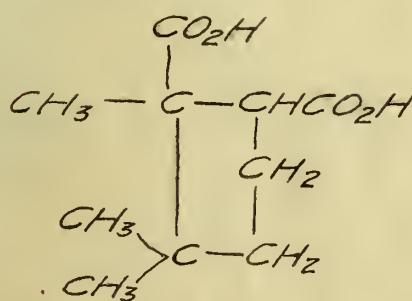


This same oxime was prepared through pentane-tetra-carboxylic ester from tri-methylene bromide and malonic ester, introducing two methyl groups (Perkins and Prentice method), saponifying, heating the tetra-carboxylic acid to 200° and distilling the resulting dimethyl pimelic acid with lime, and converting the ketone to the oxime.

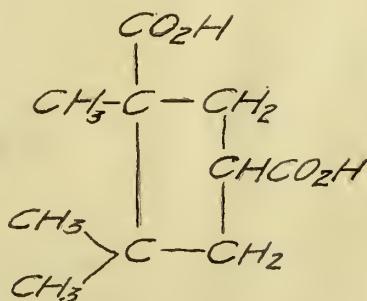
In a different way Noyes and Shepherd prepared the same ketone (Am. Chem. J., Vol. 22, p. 264), in which they distilled alpha-hydroxy-dihydro-campholytic acid with lead dioxide and sulphuric acid. In the same paper they demonstrated that the ketone had the structure



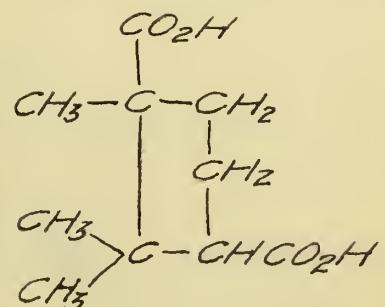
and corresponded to Bouveault's formula for camphoric acid and opposed Perkin's formula. The three formulas already proposed for camphor are:



Bouveault



Perkins



Bredt

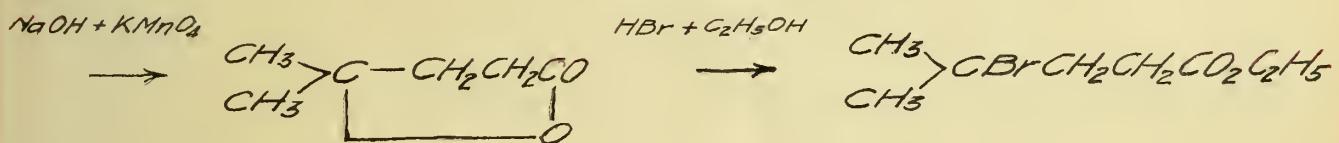
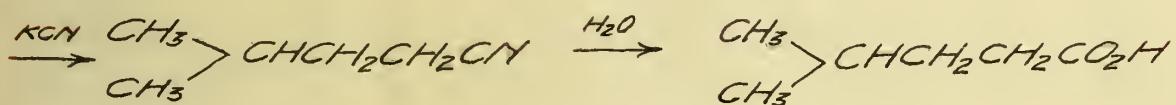
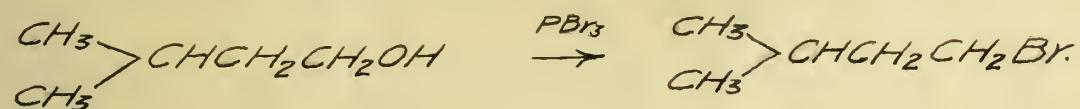
The synthesis of this ketone, so important in its relation to camphor and camphoric acid, was at once begun. W. A. Noyes, (J. Am. Chem. Soc. Vol. 25, p. 592), proposed and developed the synthesis by converting iso-amyl alcohol successively into the bromide, cyanide,



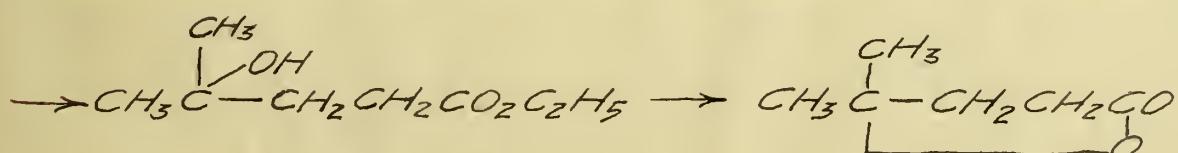
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acid, the corresponding lactone, and followed by the formation of the chlor-ester and then its condensation with cyanacetic ester.



In this procedure, the operations are so difficult, using large quantities, and the separations so tedious, that a much easier, simpler, and much less expensive method was found in the production of the isocaprolic lactone, shortening the time and producing quite satisfactory yields. The method consisted in treating levulinic ester with methyl-magnesium-iodide according to Grignard



in an apparatus later described and used. In the separation, not the hydroxy acid, as one would expect, but the lactone direct is obtained. (Annales de Chimie et de Physique, Vol. 557, p. 551 and 559).

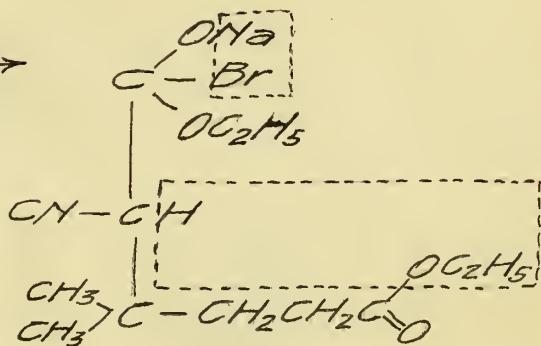
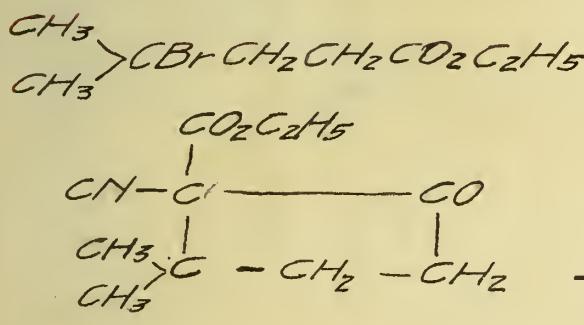
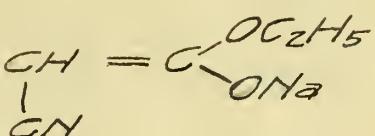
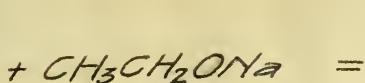
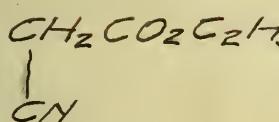
In the condensation to prepare dimethylcyanoacetoethylcyclopentanone, amounts proportional to molecular weights were used. The

sodium is dissolved in absolute alcohol, the cyanacetic ester added, followed by the chlor-iso-caproic ester, and the mixture boiled on the water bath for two hours. The acid solution was extracted with ether, the ethereal solution dried and distilled under reduced pressure and the solid remaining crystallized from absolute alcohol. Better results were obtained by using a freezing mixture of hydrochloric acid and finely shaved ice, in the use of which a large part of the ketone separated out - observations seemed to show that the ketone was decomposed upon the long heating necessary to distillation.

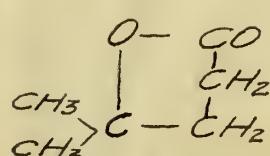
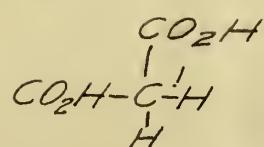
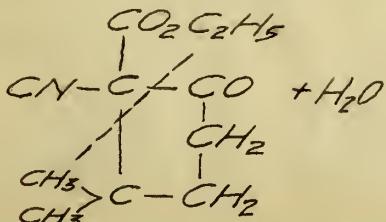
In the condensation, using the chlor-iso-ester, the yield from twenty grams was extremely poor and the needle like crystals could not be separated in pure form owing to their contamination.

An attempt was made to prepare the compound through the use of the mercury-magnesium amalgam according to Meunier and described by Noyes and Kyriakides (*J. Am. Chem. Soc.* Vol. 25, p. 1058), which consisted in adding 25 cc. absolute alcohol to the amalgam formed by heating 100 grams of mercury with 1.2 grams of magnesium, followed by the addition of 16 grams of malonic ester and 16.6 grams of chlor-iso-caproic ester. After boiling for twelve hours on the water bath, the alcohol was partially distilled under reduced pressure, and the solution, made acid with dilute sulphuric acid, extracted with ether, the ethereal solution dried with anhydrous sodium sulphate and distilled under reduced pressure. The lower boiling portion contained ether. The remaining portion distilled over at 95° to 110° and 25 mm. pressure and consisted of malonic ester and chlor-iso-caproic ester, while there was no evidence of the presence of 5,5 diethyl-2,2-dicarboxethyl cyclopentanone, which we wished to obtain.

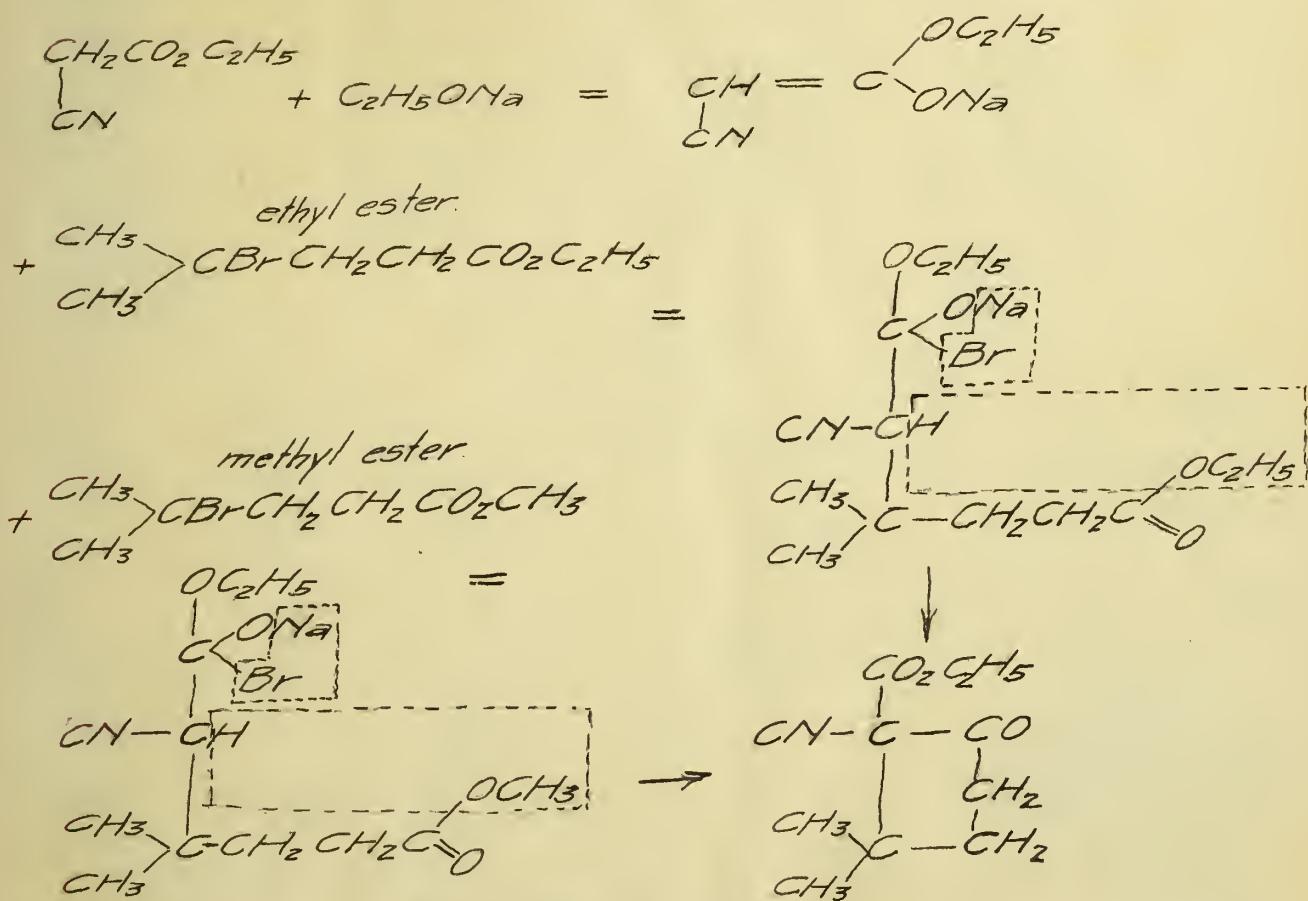
In the condensations, the brom-iso-caproic ester gave much better results than did the chlor-iso ester. The reactions involved are:



Dimethylcyanocarboxethylecyclopentanone (Am. Chem. J. Vol. 22, p. 259. Vol. 25, p. 155) crystallizes in white needles, melting at 148°S , soluble in hot alcohol, crystallizing out on cooling and insoluble in water. When heated with water in sealed tubes at 150° for three hours, the nitrile group is saponified and dimethyl-dicarboxethyl-cyclopentanone, containing no nitrogen, is formed, although it has not as yet been separated pure. Heated with hydrochloric acid, the decomposition gives carbon dioxide, acetic acid and isocaprolactone, (J. Am. Chem. Soc. Vol 25, p. 596), while saponification with alcoholic potassium hydroxide gives malonic acid and isocaprolactone. This manner of decomposition, while not singular, is peculiar in that the ring breaks and a O-atom replaces a C-atom.

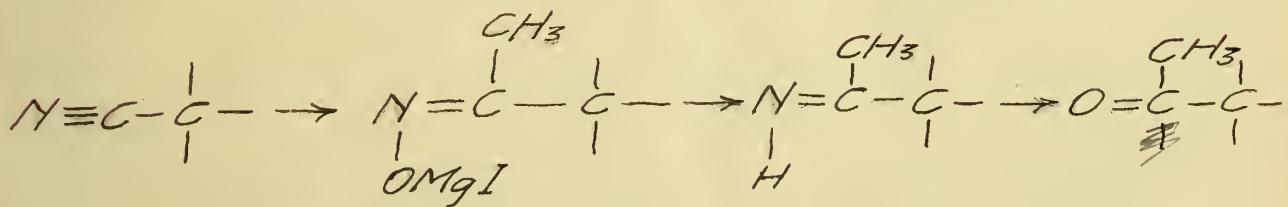
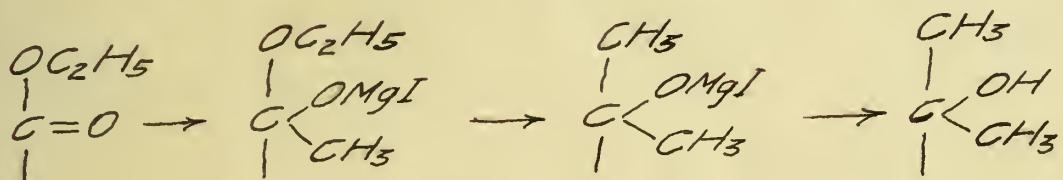
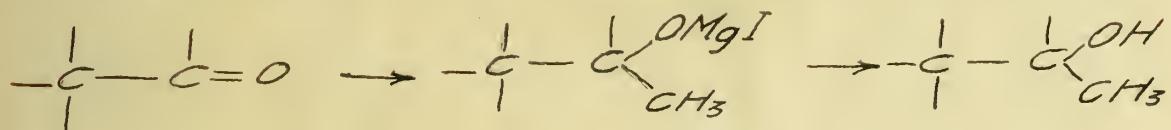


The condensation of the gamma-chlor-iso-caproic ester with the cyanacetic ester and sodium ethylate is described in Am. Chem. J. Vol. 22, p. 259, while its structure follows from the fact that the methyl ester of the brom-iso-caproic acid in the condensation gives identically the same ketone and is explained by the following reactions.



The action of Grignard's organo-magnesium compound upon the ketone was studied, using the method as described in *Annales de Chemie et de Physique*, Vol. 557, p. 561. The apparatus consisted of a short-necked round bottom flask, holding a protected reflux condenser, a dropping funnel with a conveniently bent stem and a syphon bearing a stopcock leading over into a similar flask with a bulb tube opening. All openings were protected from carbon dioxide and moisture by soda-lime and calcium chloride tubes.

Methyl-magnesium iodide may react with the three groups - CO, $\text{CO}_2\text{C}_2\text{H}_5$ and CN- of the ketone according to these reactions:-



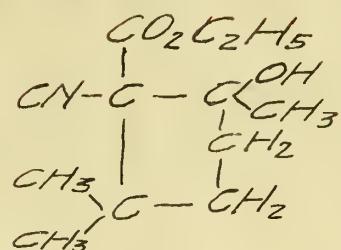
In similar condensations, the ketone group reacts before or simultaneously with the carboxethyl, while the relationship to the CN-group is undetermined. In this condensation, the ketone was treated proportionately with one mole of the methyl-magnesium-iodide to one mole of the ketone.

In the operation, 1.42 grams of methyl iodide in 25 cc. absolute ether was dropped onto 0.24 grams of magnesium covered with ether; the methyl-magnesium-iodide formed was slowly syphoned into 2.15 grams of the ketone in 25 cc. of absolute ether, and 25 cc. more of ether syphoned over to wash the syphon. The solution was made acid, extracted with ether and the ethereal solution and ether extract dried with anhydrous sodium sulphate, and the ether distilled at ordinary temperature.

The product was washed with anhydrous ether. Yield about 0.6 to 0.7 grams. Analysis of the product gave

Found
C 64.3
N 6.01
H 8.50

Calculated for
C 64.1
N 6.22
H 8.45



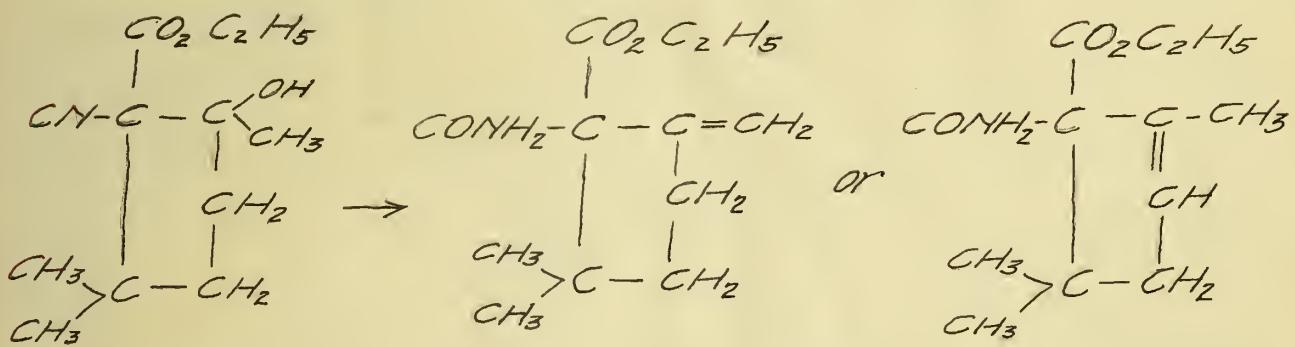
The product crystallizes in fine white crystals, melting at 195°4, and is only slightly soluble in absolute alcohol and a trifle less so in absolute ether.

The melting point of the 1-methyl, 5,5, dimethyl-cyan-carboethyl cyclopentanal was 195.4° but after the substance was cooled and the melting point again determined, it was found to be 146°. The residue in the melting point capillary was placed on a watch crystal, finely powdered, and one cc. of water added. The solution decolorized dilute potassium permanganate- hence from time to time was decolorized as more and more of the substance went into solution.

0.0557 grams of the substance was heated in a small weighed ignition tube in the sulphuric acid melting point bath to 195°, when it melted and was held at this temperature for 5 minutes, allowed to cool to 100° and then the tube was transferred to a desiccator and then reweighed. A small part of the substance had sublimed upon the side of the tube but the heating produced no evidence of moisture nor had the substance lost weight. Heating had produced a slight darkening but all the substance went into solution with absolute alcohol. The melting point of the residue after evaporation was 146°.

It was at first thought that the unsaturation was due to the loss of water from the alcohol and the adjoining CH₃ or the CH₂, but the

quantitative results disproved this. It was then thought that the water, splitting off first, had added to the $\text{C}=\text{O}$ -group to form the acid anhydride, and leaving the substance unsaturated. While this latter supposition is perhaps correct, and its demonstration more or less easy, it was not verified because of lack of time.



1. Recrystallized, D_2O , of diethyl-2,2, di-carboxy-cyclopentanone acid.

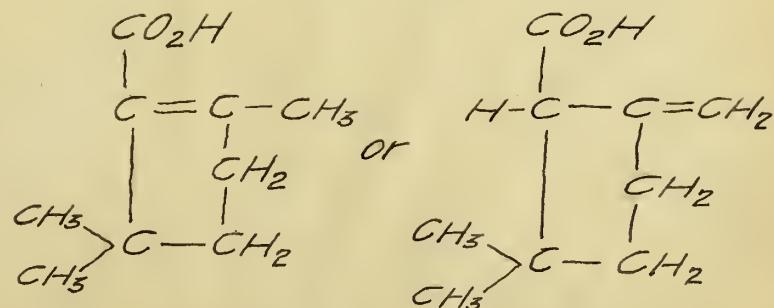
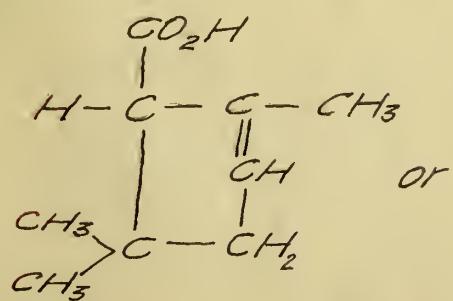
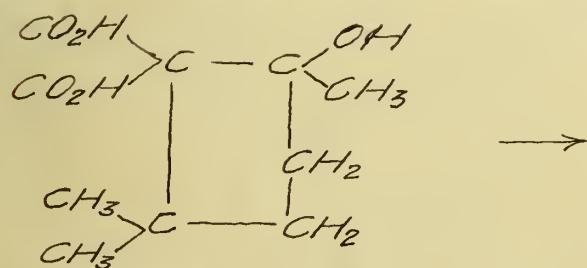
0.1010 grams of the 1-methyl-2,2, diethyl cyan carboxyethyl cyclopentanone was heated with alcoholic potassium hydroxide for several hours on a water bath in a crystallizing dish. Ammonia was given off as evidenced by a strip of litmus paper on the watch glass cover. The alcohol was allowed to boil away, ether and sulphuric acid were added and the solution was extracted several times with ether. The ethereal solution was dried over anhydrous sodium sulphate and evaporated spontaneously. A heavy brown yellow oil remained, quite soluble in absolute alcohol and absolute ether. This substance was dissolved in absolute alcohol, water added and the solution titrated with 0.1074 normal potassium hydroxide, using phenolphthalein as an indicator. The titration required the equivalent of 3.69 cc. of the tenth normal potassium hydroxide. Calculated for the dibasic acid $\text{C}_8\text{H}_{13}(\text{OH})(\text{CO}_2\text{H})$ corresponding to 0.1010 grams of the cyclopentanone derivative, 3.96 cc. is required.

The alkaline solution was evaporated to dryness, ether added, the

solution made acid with dilute sulphuric acid, and the extraction repeated. Titration of the remaining substance required the equivalent of 6.59cc. of the tenth normal alkali.

Upon recovery the second time and allowing to stand for a few days with a small crystal of sodium sulphate, the yellowish product assumed a crystalline form. These crystals when added to a freshly saponified portion of the cyan alcohol derivative, immediately deposits crystals from the yellowish brown residue, showing that the substance 1 ethyl, 5,5-dimethyl, 2,2, dicarboxy cyclopentanedic acid is a white crystalline compound and not the yellowish brown oily substance as was supposed.

The substance was heated in a small ignition tube in a sulphuric acid melting point bath to 30° when it began to decompose, giving off carbon dioxide as evidenced by lime water. The residue decolorized permanganate and showed white crystals of the dibasic acid. The heating in driving off the carbon dioxide from the dibasic acid had evidently driven off a molecule of water, producing one ketone as illustrated by three possibilities in which the water may have split off.



There is a decided difference in the stability of the ketone and corresponding alcohol derivatives. The ketone derivatives toward water are very unstable and break up, giving malonic acid and isocaprolactone and hydroxyisocaproic acid. The corresponding alcohol derivatives, however, do not so react. This stability is of interest and furnishes a means by which this class of substances may be studied.

While this investigation has been only introductory, it is hoped that the work may be continued and larger quantities of the substances prepared so that a more complete study of the different compounds may be made. On the whole, this bit of research has been quite interesting and while only able to make suppositions from the work done, definite conclusions could be formulated in a more complete investigation by following in the field as taken up.



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